Seasonal Variation in the Time to Pregnancy: Avoiding Bias by Using the Date of Onset

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To study seasonality in human fecundability, measured indirectly by time to the first pregnancy, we used data from 18,970 French-Canadian women who married for the first time during the 17th or 18th century. The time to pregnancy was approximated by the interval between marriage and first birth minus 38 weeks. We used the week of marriage and the week of conception as references to study seasonality. We found a minor seasonal pattern in time to pregnancy when using the week of marriage as a reference. The proportions of women with a short time to pregnancy were highest during December-January and June-July, indicating that these may be the most fecund periods. In contrast, we found an obvious seasonal pattern when using the date of conception as a reference. This pattern can be largely explained by a strong seasonal pattern in pregnancy planning (in this case, in marriages). When studying seasonal variation in the time to pregnancy, the date of onset of the time to pregnancy should be used as reference, not the date of conception. Otherwise, results will be biased owing to seasonality in pregnancy planning. The same is true for studies on seasonally bound exposures in relation to time to pregnancy. (Epidemiology 1996;7:156–160)

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Seasonal reproduction is a common phenomenon in many animals. In humans, seasonal variation can also be observed for several reproductive factors, for instance, ovulation,[1,2] spermatozoa concentration,[3] pregnancy after artificial donor insemination,[4–7] early pregnancy loss,[8] and birth.[9–11] A seasonal pattern may be caused by photoperiodicity, which influences gonadal function. Information about the gonadal function of women can be derived from gonadal hormone production and ovulation. This information is difficult to gather, however. A more convenient, although indirect, measure of gonadal function is fecundability. The time to pregnancy can be considered as an indication of fecundability.[12]

For studying seasonality in the time to pregnancy, a date of reference should be defined. Either the date of the onset of the time to pregnancy (that is, the first day of refraining from any kind of contraceptive method because of pregnancy wish) or the date of the end of the time to pregnancy (that is, the date of conception) can be used. In this study, we used proxies for both definitions.

This article addresses the question of whether there is seasonal variation in the time to pregnancy. Data were obtained from a historical cohort of women who lived in Quebec during the 17th and 18th centuries. As contraceptive methods were not accessible in those days (with the exception of total abstinence from sexual intercourse), the date of marriage can be used as the date of the onset of the time to the first pregnancy. We approximated the end of the time to pregnancy by the date of the first birth minus 38 weeks for the gestational period. In addition, we studied the occurrence of bias related to the choice of the date of reference in studies on variation in the time to pregnancy.

Subjects and Methods

Family reconstitutions of the early French-Canadians are being compiled in the form of a population register called "Le registre de la population de Québec ancien" by the Programme de recherche en démographie historique at the University of Montreal.[13] The register covers the entire population from the arrival of the first settlers in the early part of the seventeenth century to 1765, after the British takeover. This population can be considered to have lived in conditions of "natural fertility," that is, free from any contraceptive practice.[14]

In this study, we used the interval between the date of marriage and the date of birth of the first child minus 38 weeks as a proxy for the time to pregnancy. We included women in the study if the dates of their marriage and first birth were known and if the interval between their

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marriage and first birth was at least 240 days and, at most, 1,096 days. We used the lower limit of 240 days because children born within a shorter interval had presumably been conceived before marriage. The upper limit was necessary because long intervals have often been found to correspond with a birth in the family that was missed by the registry. Because of the lower limit of 240 days, the time to pregnancy was below zero in some cases.

To study seasonality, we used both the week of marriage and the week of conception (approximated by the week of the first birth minus 38 weeks) as the date of reference. For reasons of simplicity, marriages or births on the 29th of February or on the 31st of December were excluded from the analyses based on the week of marriage or the week of conception, respectively (leading to exactly 52 weeks per year).

As seasonal influence would be the most obvious during the first menstrual cycles after marriage, because long intervals will dilute the influence of the season, we performed analyses to detect seasonal patterns in the time to pregnancy of ≤0, ≤1, ≤2, or ≤3 months. The weeks were entered into a logistic regression model as a sine function with a period of 26 weeks or 52 weeks with variable amplitude and shift. We chose the best fitting model as the one with the highest likelihood ratio. Additionally, we calculated the deviance to determine whether the observed proportions of pregnant women per week were equal to the expected proportions when using the model with the best fitting sine function. We also used logistic regression analysis to correct for possible confounding effects of the woman's age at marriage (in three age groups) and the calendar year (in categories of 10 years and, in one case of small numbers, in a 20-year period).

Results

Data were available from 20,888 women. Only the first marriage was included in the analysis (N = 18,970). The age of the women at first marriage varied from 11 to 46 years. Half of the women married before the age of 21. Their marriages had taken place between 1634 and 1762.

Half of the women conceived within 3 months. The time to pregnancy varied with the age of the women: the youngest women (18 years or younger) and the oldest women (34 years or older) had the longest time to pregnancy. Moreover, the time to pregnancy tended to be the longest during the first decennia of French settlement in Canada.

The proportions of women with a time to pregnancy of ≤0, ≤1, ≤2, and ≤3 months per week of marriage and the best fitting sine functions are shown in Figure 1. A sine function with a period of 26 weeks fitted better than one with a period of 52 weeks. There was only small variation in the proportions of women who became pregnant within 0, 1, 2, or 3 months: for ≤0 months from 4.5 to 6.4%, for ≤1 month from 22.9 to 27.3%, for ≤2 months from 38.9 to 45.0, and for ≤3 months from 51.6 to 54.8%. Because of the large number of observations, these seasonal patterns in the time to pregnancy deviated from a uniform distribution ($P < 0.002$ in most cases). Peaks in the bimodal curves were found during weeks 50–2 (December-January) and weeks 24–28 (June-July). The deviance (df = 49) was 76.97 for ≤0 months ($P = 0.01$), 69.09 for ≤1 month ($P = 0.03$), 58.93 for ≤2 months ($P = 0.16$), and 40.65 for ≤3 months ($P = 0.80$). These results indicated that the proportions of pregnant women per week of marriage could be predicted well with the sine function models with a period of 26 weeks. Adjustment for the effects of age at the time of marriage and the calendar period did not change the results to any substantial extent.

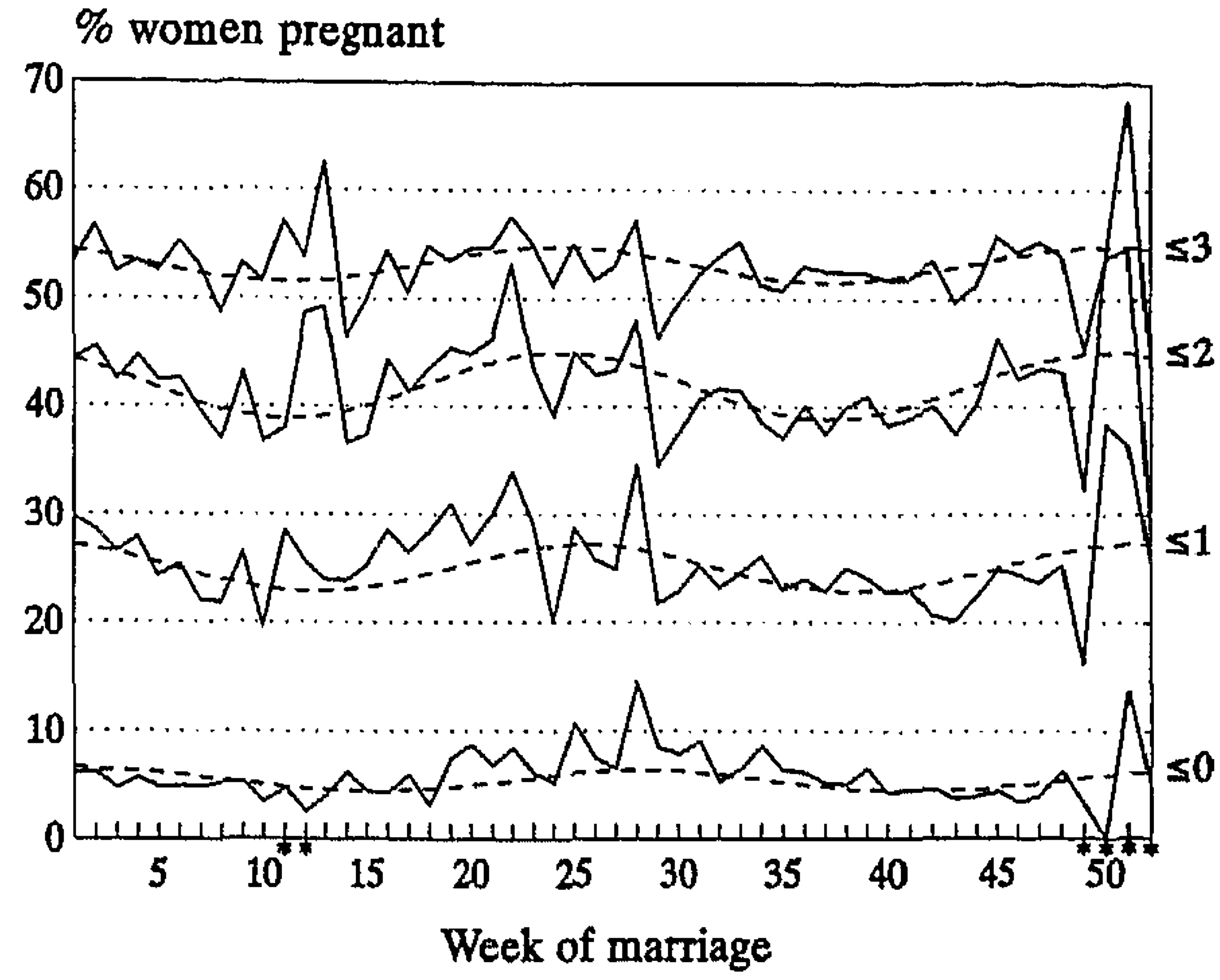

FIGURE 1. Percentages of women with a time to pregnancy of ≤0, ≤1, ≤2, or ≤3 months, per week of marriage; crude data and best fitting sine function (excluding marriages on the 29th of February or the 31st of December). * = weeks with fewer than 50 marriages.

In contrast, when we used the week of conception as the date of reference, an obvious unimodal seasonal pattern was observed in the time to pregnancy (Figure 2). A sine function with a period of 52 weeks fitted better than a sine function with a period of 26 weeks. The deviance for the proportion of women with a time to pregnancy of ≤0, ≤1, ≤2, or ≤3 months was 312.12, 698.75, 248.92, and 106.63, respectively (df = 49, $P < 0.0001$). Thus, although the model with a sine function with a period of 52 weeks explained much of the variation in the distribution of the time to pregnancy throughout the year (likelihood ratio test result in all cases $P < 0.0001$), it did not predict the observed proportions very well. Moreover, the seasonal patterns in the time to pregnancy per week of conception remained after adjustment for confounding by age and calendar period.

Thus, the results of the two approaches for studying seasonality in the time to pregnancy differed considerably. The reason for this can be found in a seasonal pattern in marriages (Figure 3). The majority of women married during weeks 1–8 and 41–48 (that is, January-February and October-November). Because half of the

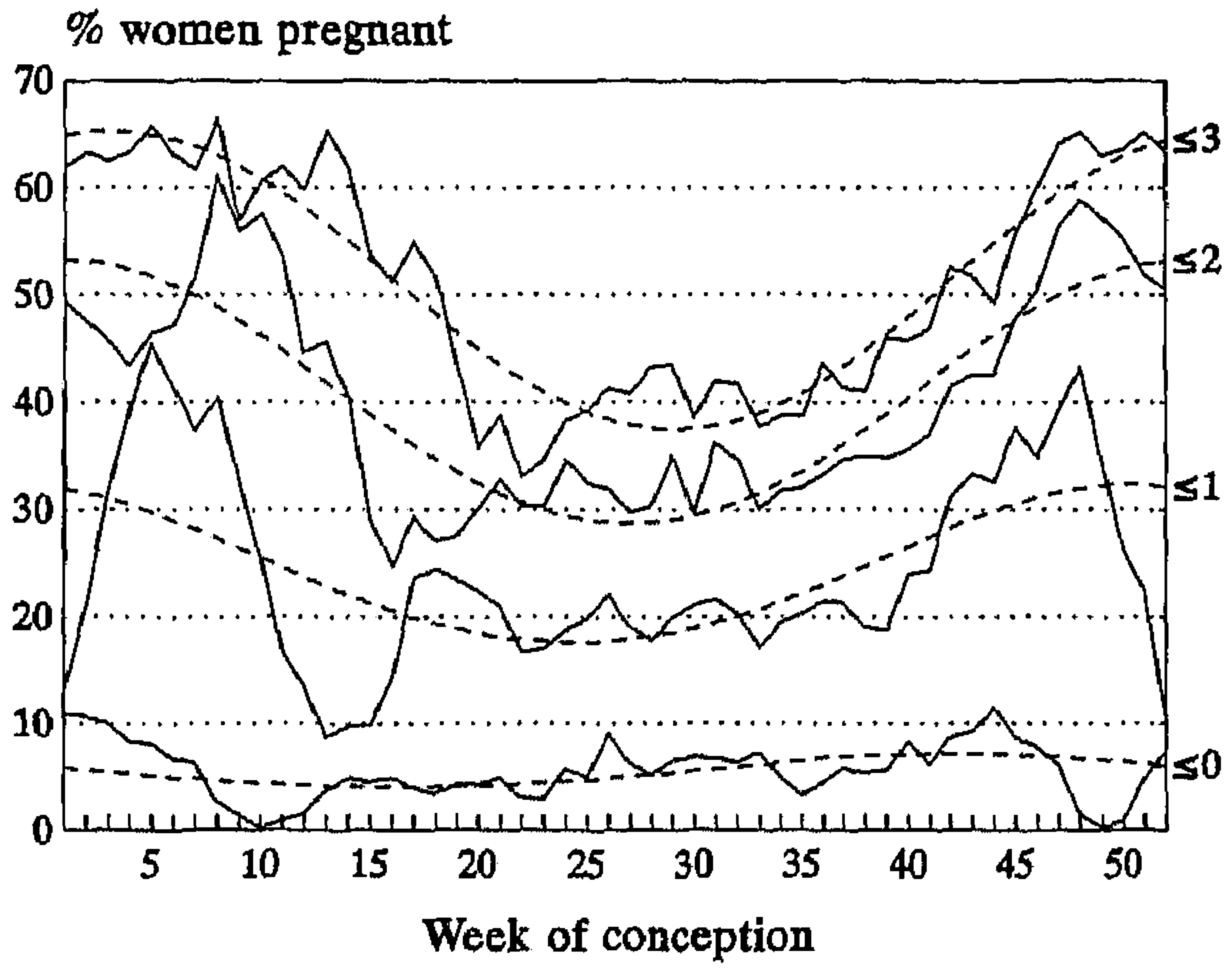

FIGURE 2. Percentages of women with a time to pregnancy of ≤0, ≤1, ≤2, or ≤3 months, per week of conception; crude data and best fitting sine function (excluding births on the 29th of February or the 31st of December).

women conceived within 3 months after marriage, a peak of conceptions followed during weeks 45–10 (November-mid-March) (Figure 4). The expected number of conceptions per week with a time to pregnancy of ≤0, ≤1, ≤2, or ≤3 months could be estimated by using the number of marriages per week (Figure 3) and the distribution of the time to pregnancy in the population. It appeared that the high proportion of women with a relatively short time to pregnancy after having conceived during the weeks 45–10 (Figure 2) was explained to a large extent by the distribution of marriages during the year. (For the four curves shown in Figure 2, the model χ^2 (df = 51) decreased from values of higher than 355, when assuming a uniform distribution, to values of 99 or less, when taking into account the distribution of marriages (Figure 3) and the time to pregnancy.)

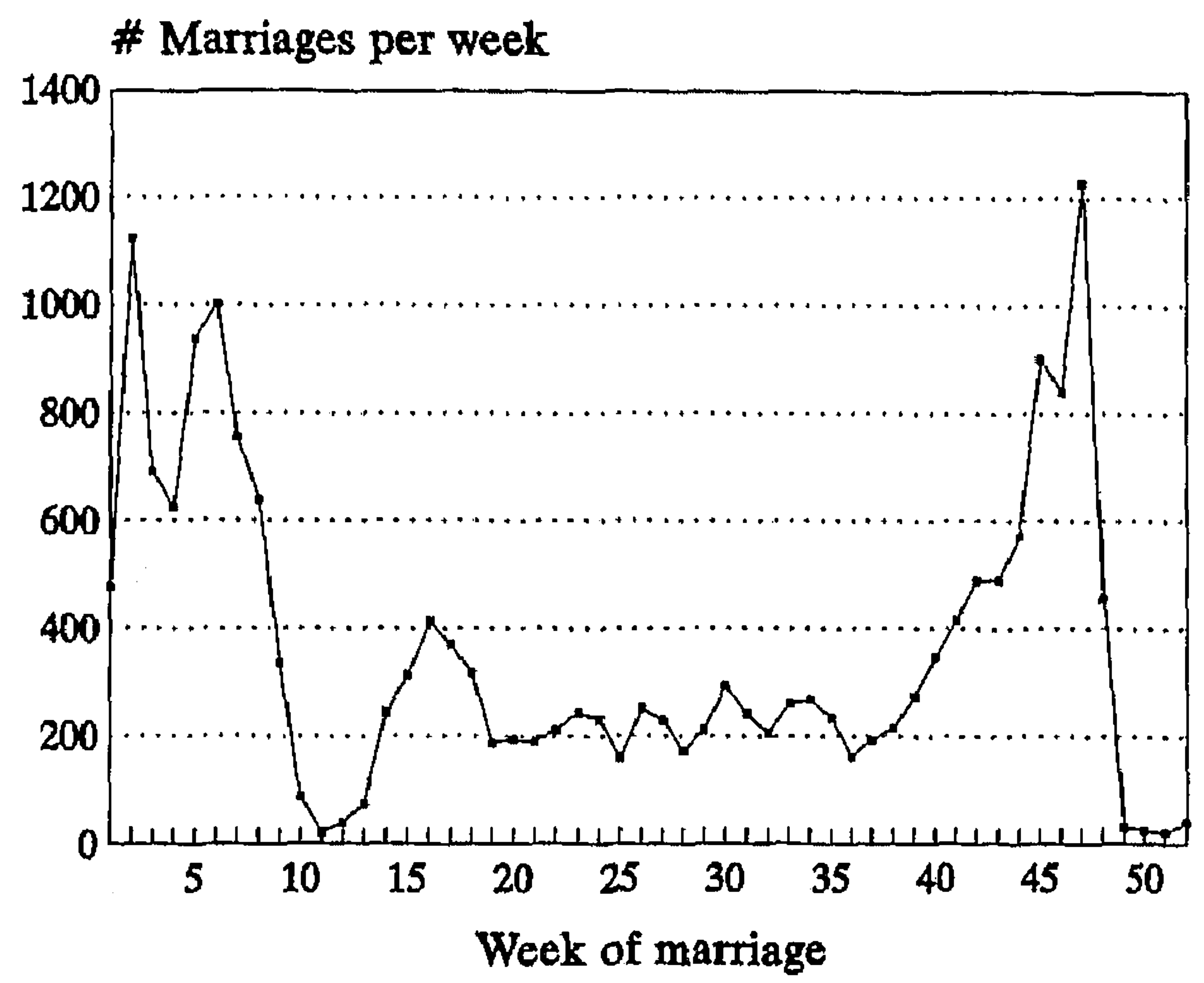

FIGURE 3. Number of marriages per week (excluding marriages on the 29th of February or the 31st of December).

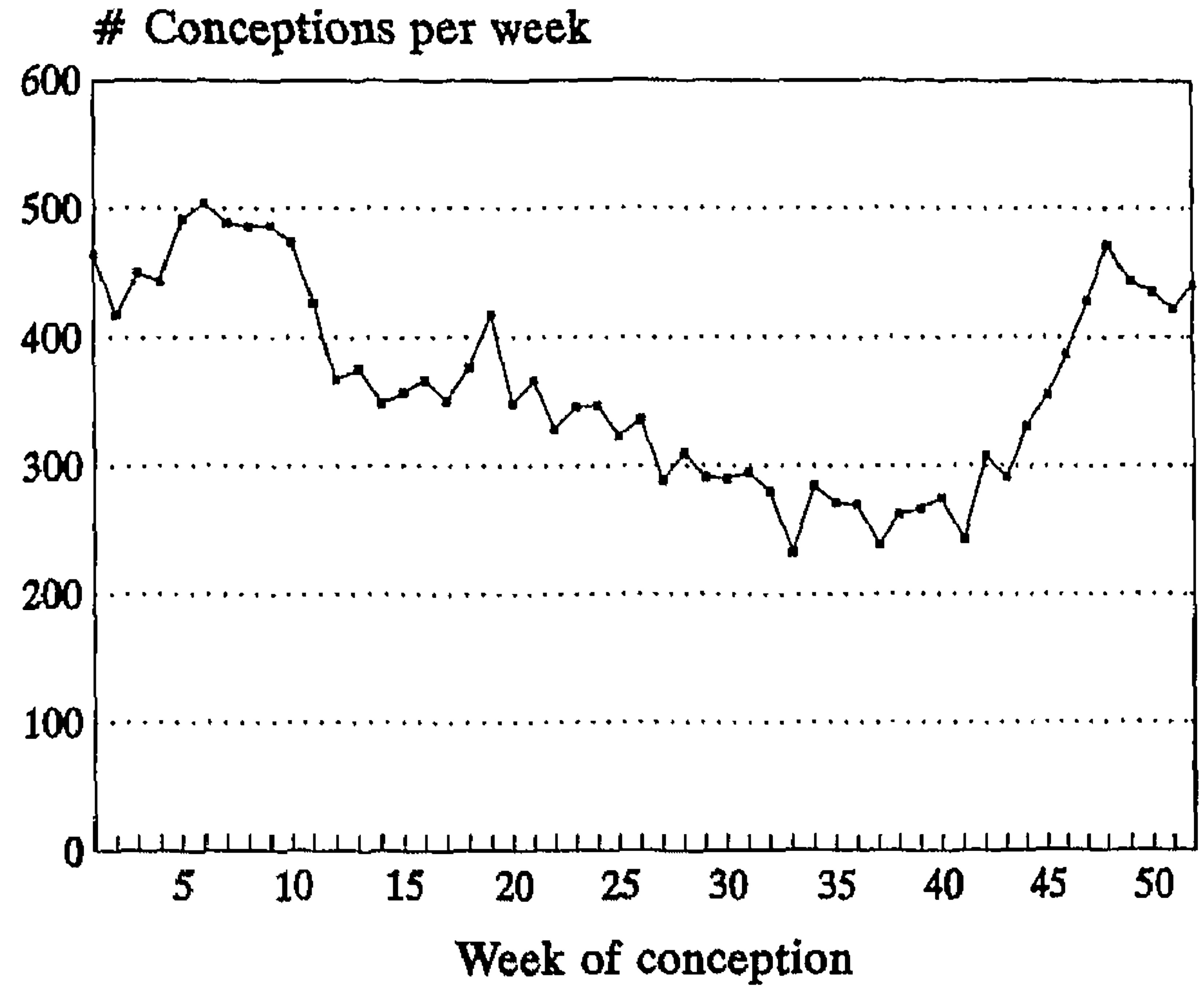

FIGURE 4. Number of conceptions per week (excluding births on the 29th of February or the 31st of December).

Discussion

As seasonal changes in, for instance, the photoperiod may cause a seasonal pattern in gonadal function and thus in fecundability, we focused on the question of whether there was a seasonal pattern in the time to pregnancy. The season was defined in two ways, that is, by the onset and by the end of the time to pregnancy. Although almost no seasonal pattern was observed in the time to pregnancy when the date of onset was used as the point of reference, we found a striking seasonal pattern when the end of the time to pregnancy, that is, the week of conception, was the reference point. In this case, the seasonal variation in the time to pregnancy was explained by the seasonal pattern in marriages. Because 53% of the women became pregnant within 3 months, the marriage pattern almost dictated the conception pattern and thus the relation between the time to pregnancy and the date of conception.

We found the highest proportions of women with a short time to pregnancy among those who married in December-January or in June-July. This finding may indicate that gonadal function is optimal during these periods. With a part of the same database used here (N = 5,194), Nonaka *et al*[15] found that marriages in August-October resulted in a lower percentage of immediate conceptions (8–10 months after marriage) than in other seasons. Although this finding agrees with our results, Nonaka *et al* did not find a bimodal pattern. A possible explanation for the difference is that we used a database three times as large and studied seasonality in weeks instead of in 3-month periods. In Finland, Timonen *et al*[1] found the highest proportion of ovulations during the "light season," that is, around June. Rameshkumar *et al*,[2] in contrast, found the highest proportion of anovulations during the same period in India. These conflicting patterns, however, may be explained by the influence of both the photoperiod and temperature.[11] Spermatozoa concentration was found to be the highest during February and March and almost as high in November; other semen characteristics did not reveal a seasonal pattern.[3] In ovulating women who underwent artificial insemination by donor, the highest conception rates were found during October-March in England[4] and in October-January in Finland.[5] Unfortunately, the proportion of ovulating women per month were not reported in these two studies. In another Canadian study, Henderson-Toth *et al*[7] found the highest pregnancy rate after artificial insemination during November-December and February; they did not mention whether they excluded anovulatory cycles. Thus, although none of these other studies found a bimodal pattern, the indication in our study for a peak in fecundability during June-July was in agreement with the ovulation pattern found in Finland by Timonen *et al*,[1] whereas the peak in fecundability during December-January was in agreement with observations found in sperm concentration and after artificial insemination by donor.

A factor that possibly influences the seasonal pattern in the time to pregnancy might be seasonal variation in pregnancy loss. We lacked information to evaluate this issue. Several other studies found seasonality in spontaneous abortions when using births as a reference.[16–18] As seasonal variation in abortions can influence the number of births, the results of those studies may be biased. Two prospective studies provide further insight. Weinberg *et al*[8] found peaks in the risk of early pregnancy loss (within 6 weeks after the last menstrual period) in 221 women with a positive pregnancy test result after having conceived in early September to early December. Nakamura *et al*[19] observed 11 spontaneous abortions in 519 women who had undergone ultrasonographic examination for confirmation of pregnancy. The last menstrual periods were more frequent during July-December (8/328) than during the first half of the year (3/189). The relatively high probability of pregnancy loss at the end of the year in these two studies seems to contradict the high proportion of women with a short time to pregnancy around December-January in our study. This discrepancy may indicate that the seasonal pattern in the time to pregnancy found in our study was not caused by a seasonal pattern in pregnancy loss.

To study a biological phenomenon that influences fecundability, it is correct to use the date of the onset of the time to pregnancy as a reference. In this case, the impact of a seasonal pattern in marriages or in pregnancy planning in general can be found only in the precision of the measured time to pregnancy per week of marriage; it cannot lead to bias. An important consequence of seasonality in pregnancy planning is the potential for biased results in studies on a seasonally bound exposure (for example, in an occupational setting) in relation to the time to pregnancy. This bias may occur if the exposure status is measured at the date of conception instead of at the onset of the time to pregnancy. This type of "time bias" differs from the one discussed by Weinberg *et al*,[20,21] who related it to changes in exposure status over calendar time.

To overcome bias because of pregnancy planning, the onset of the time to pregnancy should be used as the date of reference. The best information would be obtained from a prospective study, in which women are enrolled in the study before they begin their time to pregnancy. This type of study, however, would have to cope with considerable practical problems connected with the large number of women who should be followed for a long period. An alternative is a retrospective study in which the date of the onset of the time to pregnancy is known. With such a study, the bias of pregnancy planning can be resolved. Unfortunately, if women are enrolled in the study while they are pregnant or after delivery, the date of the onset of the time to pregnancy and the date of conception will often be unknown, and subfecund women will be underrepresented. The result will be underestimation of the strength of the relation, but no change in the direction of the effect estimators. In this study, the date of marriage was a reliable proxy for the onset of the time to pregnancy, because contraceptive methods were not accessible in the 17th and 18th centuries. Moreover, bias because of missing data of marriages or births is not likely, because the register is nearly complete, and the population was essentially closed.[13]

We conclude that the impact of a biological factor in causing seasonal variation in the time to pregnancy and thus in fecundability, is small; the most fecund periods seem to be December-January and June-July. Moreover, to study this correctly, the onset of the time to pregnancy should be used as the date of reference, not the date of conception.

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